SHOOK, HARDY & BACON

ADULT ASTHMA

Definition: Although asthma has a variety of definitions, common characteristics include the following: 1) airway obstructions that are reversible, either spontaneously or with treatment; 2) airway inflammations; and 3) increased airway responsiveness to a variety of stimuli.

Clinical Assessment: Typical clinical measures of asthma incidence and severity of episodes includes spirometry and lung function tests. These measures are considered to be objective yet may not necessarily be so; psychological factors can influence performance in clinical tests.

Incidence: Asthma incidence in the United States has increased. Reports indicate that from 1980 to 1987 there was a 43% increase in the number of diagnosed cases of adult asthma. Asthma mortality has increased from 0.8 per 100,000 in 1977 to 2.1 per 100,000 in 1991.

Experimental Studies:

- There are seven laboratory studies that examine the effects of ETS on asthmatic individuals. [See Appendix III for a summary of results.]
- Results of two studies suggest that there may be a relationship between ETS exposure and decreases in lung function, however, these studies are small, do not adequately control for psychological factors, and utilize exposure levels to sidestream smoke at extremely high concentrations.
- Four of the studies were inconclusive in terms of the objective measures of lung function even though the subjects reported responses to ETS exposures.
- One study reported significant decreases in lung function for 7 of 21 subjects at high ETS concentrations; only two subjects had significant decreases at lower ETS concentrations.
- Subjects from all seven studies reported subjective responses to ETS that include eye irritation, nasal discomfort, shortness of breath, wheezing, and chest tightness.
- Experimental studies of ETS exposures in the laboratory have three primary shortcomings: 1) they fail to utilize the

appropriate material (aged sidestream smoke was the "best" attempt at simulating ETS exposures), 2) they tend to utilize extremely high ETS concentrations (CO levels > 25-30 ppm), and 3) they fail to control for psychological factors (ETS odor).

Epidemiology Studies:

- There are four U.S. population surveys that address ETS exposure among adult asthmatics. Results from these studies are mixed: two studies suggest a possible relationship between ETS exposure and asthma episodes, two studies report no effects of ETS exposures on symptoms or pulmonary function.

- The two studies that report significant risk of asthma episodes from ETS exposure were extremely weak associations (RR < 1.5) and failed to adequately control for the multitude of confounders that have been postulated as asthma irritants.

- Dietary confounders that have been hypothesized to be related to asthma exacerbation include: low vitamin C intake and food allergies.

- Problems with the population studies include the following: 1) inadequate measures of exposure (self-reports), 2) inadequate control of confounders, 3) failure to confirm asthma diagnoses, 4) subjective measures of airway reactivity, and 5) use of subjects who are current or exsmokers.

- Witorsch reviewed the epidemiologic literature on ETS exposure and adult asthma and concluded that both acute and long term effects of ETS exposure are inconclusive.

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WORKPLACE ETS ASTHMA ISSUES

- There are two categories of asthma that relate to the workplace: work-aggravated asthma and occupational asthma.

Work-Aggravated Asthma

- Work-aggravated asthma is preexisting asthma that is aggravated by chemical or physical irritants in the workplace. In many ways, symptoms and "causes" are similar to those which characterize Sick Building Syndrome and Building Related Illness.

- Individuals reporting work-aggravated asthma experience symptoms during and immediate following work, but the symptoms are alleviated soon after leaving the workplace. Long term, chronic aggravation can extend the duration of symptoms so that they are not alleviated by leaving the workplace.

- Examples of indoor air constituents that have been reported to increase symptoms of asthma include, but are not exclusive to: ozone, nitrogen oxides, carpets, dust, biological allergens (dust mites, pets, cockroaches, bacteria, molds, etc.), colognes, and ETS.

- One of the epidemiology studies (see above) reported a significant increase of asthma symptoms associated with ETS in the workplace. However, the data were subjective (a population survey) and lacked resolution (number of years worked with a smoker grouped into ten year increments).

- No other epidemiologic studies have focused specifically on workplace issues (N.B. Presumably, there are other studies that will be listed in the LSI search results.)

Occupational Asthma

- Occupational asthma is asthma that is specifically caused by conditions in the workplace and typically occurs following high level concentration exposures to specific chemical and physical substances (e.g., cotton dust).

- Occupational asthma can occur in individuals with preexisting asthma.

- Appendix IV gives examples of U.K. incidence rates (Table 17-1), U.K. incidence rates by cause (Table 17-2), animal causes

(Table 17-3), vegetable causes (Table 17-4), and chemical causes (Table 17-5).

- ETS is not considered to be a factor in development of occupational asthma.

APPENDIX I. PM SUBMISSION TO OSHA, AUG., 1994

THE EPIDEMIOLOGIC AND EXPERIMENTAL DATA AVAILABLE DO NOT SUPPORT OSHA'S CONTENTION THAT COMPROMISED INDIVIDUALS IN THE WORKPLACE HAVE A SIGNIFICANT RISK OF MATERIAL HEALTH IMPAIRMENT BECAUSE OF EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

OSHA claims that although the pulmonary function decrements reported to be associated with exposure to ETS in

healthy nonsmokers are small and of questionable clinical significance, these changes may become significant in persons with already impaired pulmonary function (e.g., asthmatics). In its attempt to substantiate this claim, OSHA references two experimental studies on adult asthmatics exposed to ETS for one hour in an exposure chamber. The first study, Knight and Breslin, 1985, reported on only six subjects, four of whom had previously given a positive history of ETS "attacks." (Ex. 8-182) The authors (and OSHA) did not discuss the possibility that psychological factors may have played a role in the subjects' reported "reactions" to the ETS exposure.

The second study, by Dahms et al., 1981, reported on ten patients with asthma (five of whom were included because they reported specific complaints when exposed to cigarette smoke) and ten normal patients. (Ex. 8-76) While the authors reported an association between exposure to ETS and lung function responses in the asthmatic subjects, they reported that "not all subjects showed the same pattern of pulmonary responses to the smoke exposure." The authors also reported that "we were not able to exclude the possibility that these changes in pulmonary function were emotionally related to cigarette smoke" [emphasis added]. Similarly, the 1986 Surgeon General's report recognized that "in this study, subjects were not blinded as to the exposure and were selected because of complaints about smoke sensitivity."

OSHA also references a 1991 review article by Stanton Glantz and Richard Daynard (Tobacco Liability Project) which makes several claims regarding exposure to environmental tobacco smoke, none of which is supported by a thorough and critical review of the scientific literature available. (Ex. 3-438D)

OSHA claims that asthmatics are believed to be especially sensitive to various environmental influences, including ETS, but a thorough review of the scientific data on ETS does not convincingly support this contention. There are currently ten major studies on ETS exposures among adult asthmatics. Seven of the studies are clinical in nature, where exposures to ETS were controlled under laboratory conditions. The other three studies are population surveys. All of the studies evaluate reports of respiratory symptoms such as coughing, wheezing, and irritation ("subjective complaints") and changes in lung function (an "objective" test for lung impairment).

Only two of the seven clinical studies report objective decreases in lung function among the majority of asthmatics exposed to environmental tobacco smoke. However, the patients in both positive studies were exposed to excessively high and unrealistic levels of ETS [15-32 ppm carbon monoxide], and, as mentioned above, the authors of one of the studies conceded that the observed effects may have been due to psychological factors. In the

remaining five clinical studies, a number of patients reportedly complained of subjective symptoms upon exposure to ETS, but objective results (i.e., evidence of airways obstruction or significant changes in lung flow rates) were not observed in the vast majority of patients.[16-20]

Data from the three population surveys on adult asthmatics are generally consistent with data reported in the majority of clinical studies.[21-23] A report of a large-scale population survey in the U.S. suggested that ETS exposures in the home did not affect either symptoms or pulmonary function in adult asthmatics. Another group of U.S. researchers recently reported that exposure to ETS did not impair lung function in the 263 asthmatic adult subjects studied. The third study reported mixed results for the development of asthma-related symptoms in individuals reporting exposures to ETS during childhood and adulthood.

OSHA FAILS TO DISCUSS THE PROBLEMS IN GENERALIZING DATA FROM "EXPOSURE CHAMBER" STUDIES TO THE "REAL-WORLD" SITUATION

As mentioned above, the conditions under which asthmatic patients are exposed to ETS in these studies are of questionable relevance to "real-life" exposures. The Surgeon General, in the

1986 report on ETS, conceded that exposure chamber studies may not be indicative of the "real world" situation:

> Acute exposure in a chamber may not adequately represent exposure in the general environment. Biases in observation and the in [sic] selection of subjects and the subjects' own expectations may account for the widely divergent results. Studies of large numbers of individuals with measurement of the relevant physiologic and exposure parameters will be necessary to adequately address the effects of environmental tobacco smoke exposure on asthmatics.

THE MAJORITY OF ANIMAL STUDIES REFERENCED BY OSHA ARE STUDIES OF MAINSTREAM TOBACCO SMOKE AND ARE NOT RELEVANT TO A DISCUSSION OF POTENTIAL PULMONARY EFFECTS IN NONSMOKING ADULTS EXPOSED TO ENVIRONMENTAL TOBACCO SMOKE IN THE WORKPLACE

Although OSHA refers to the studies in this section as experimental "ETS" studies, the majority of the studies are mainstream smoke studies which have little or no relevance to ETS issues. ETS is not the same as either mainstream or sidestream smoke. For a complete discussion of this issue, please refer to the section on exposure issues in this submission.

OSHA mentions isolated conclusions from several experimental animal studies but makes no attempt to explain how these data relate to real-life ETS exposures of nonsmoking adults in the workplace. OSHA also does not make any attempt to explain

the physiological or clinical significance, if any, of the reported data. Nor does OSHA address the apparent inconsistencies in the reported data. For example, "effects" may be reported in one species but not in another.

OSHA makes no attempt to explain the relevance, if any, of these high-dose experiments in animals to real-life workplace exposures in humans, even when some of the studies from which they report data acknowledge that these exposure levels are extreme when compared to the "real world" of "smoke-filled" restaurants or offices. OSHA's responsibility in this proposed rulemaking is to show that workplace exposures to ETS are likely to result in material health impairment in non-smoking adults. They have failed to substantiate this claim.

OSHA FAILS TO REFERENCE MUCH OF THE RELEVANT LITERATURE SUBMITTED IN RESPONSE TO THE OSHA RFI IN 1992

OSHA presents no critical discussion of potential confounding factors, merely stating that the studies "varied" in their consideration of such factors and that "several studies" have examined isolated variables; OSHA makes no statement regarding the adequacy of control for such factors in these studies

In the Proposed Rule, OSHA presents selected data on the possible association between exposure to ETS and decreased pulmonary function in adult nonsmokers. Philip Morris submitted much of the literature which OSHA has omitted from its Proposed Rule to the docket for the RFI in 1992. (Ex. 3-1074) For a discussion of this literature, please see the response to question 2(a)iii in Ex. 3-1074. A discussion of confounding factors, which OSHA does not provide in its Proposed Rule, is also presented in that section of Ex. 3-1074.

OSHA, while conceding that the studies on ETS exposure and pulmonary effects in nonsmoking adults "vary by numerous factors," makes no apparent attempt to explain why these variations are given no importance in their "analysis" of the literature

OSHA does not elaborate on its statement that the studies on ETS exposure and respiratory effects in nonsmoking adults "vary by numerous factors, such as the population studied, the measures

used to estimate exposure to ETS, and the physiologic and health outcomes examined." While other reviewers of this body of literature have concluded that it is difficult, if not impossible, to make any definitive conclusions from these data, OSHA attempts, but fails, to make a case for causation.

APPENDIX II. ETS LITERATURE REVIEW, JAN., 1995

Asthma

Asthmatics are believed to be especially sensitive to various environmental influences, including ETS, but the scientific data on ETS do not convincingly support this contention. There are currently ten major studies on ETS exposures among adult asthmatics.[34-43] Seven of the studies are clinical in nature, where exposures to ETS were controlled under laboratory conditions. The other three studies are population surveys. All of the studies evaluate reports of respiratory symptoms such as coughing, wheezing, and irritation ("subjective complaints") and changes in lung function (an "objective" test for lung impairment).

Only two of seven clinical studies report objective decreases in lung function among the majority of asthmatics exposed to environmental tobacco smoke.[34-35] However, the patients in both positive studies were exposed to excessively high and unrealistic levels of ETS, and the authors themselves noted that the observed effects may have been due to psychological factors. In the remaining five clinical studies, a number of patients reportedly complained of subjective symptoms upon exposure to ETS, but objective results, i.e., evidence of airways obstruction or significant changes in lung flow rates, were not observed in the vast majority of patients.[32-37]

Data from the three population surveys on adult asthmatics are generally consistent with results reported in the majority of clinical studies.[42-43] A report of a large-scale population survey in the U.S. suggested that ETS exposures in the home did not affect either symptoms or

pulmonary function in adult asthmatics.[41] Another group of U.S. researchers recently reported that exposure to ETS did not impair lung function in the 263 asthmatic adult subjects studied.[43] The third study reported mixed results for the development of asthma-related symptoms in individuals reporting exposures to ETS during childhood and adulthood.[43]

Allergy

Although some individuals claim to be annoyed by the sight and smell of tobacco smoke and a few even report experiencing irritation, the existence of human allergens in tobacco smoke has not been established scientifically. Claims about tobacco smoke allergy arise because some individuals -- usually those who experience allergic reactions to other substances such as weeds -- develop allergic skin responses from application of tobacco leaf extract or tobacco smoke condensates. However, positive skin reactions to leaf extracts or condensates have not been correlated with clinical responses to tobacco smoke exposures.[39, 44-45] Indeed, studies indicate that people who claim to be "smoke-sensitive" do not react more frequently to tobacco leaf extract than those who do not consider themselves "sensitive" to tobacco smoke.[44-46]

There are no data suggesting the existence of a specific sensitization of individuals to tobacco smoke.[47-50] This is not to deny that there are individuals, including those with pre-existent allergies, who may report annoyance and irritation in the presence of ETS. However, the basis for these reactions is neither specific nor immunologic and cannot be regarded as evidence of a genuine tobacco smoke allergy.

APPENDIX III. SUMMARY OF RESULTS OF EXPERIMENTAL ASTHMA STUDIES. (WITORSCH, 1992)

STUDY	FINDINGS
Shephard *et al*, 1979a	No effects on pulmonary function; eye irritation and to a lesser extent symptoms such as nasal discharge, wheezing, and chest tightness reported
Dahms *et al*, 1981	Linear, time-dependent decr. in FVC, FEV_1, FEF_{25-75}; incr. symptoms
Knight/Breslin. 1985	Decr. pulmonary function; incr. symptoms (eye irritation, chest tightness, wheezing); incr. sensitivity to histamine challenge
Wiedemann *et al*, 1986	No effects on baseline pulmonary function; eye irritation (before goggles), nasopharyngeal irritation, mild cough; decr. sensitivity of methacholine challenge
Stankus *et al*, 1988	Decr. (>20%) in FEV_1 in 7 of 21 subjects; Eye irritation in all subjects; nasal congestion in some subjects; cough, shortness of breath and/or chest tightness in all subjects showing physiological responses to ETS
Jorres *et al*, 1990 (abstract)	No effects on pulmonary function and bronchial responsiveness to methacholine challenge; eye irritation was only symptom
Gurk *et al*, 1991 (abstract)	4% decr. in mean FEV_1; 13% incr. in mean SRaw; no change bronchial reac. to methacholine in asthmatics as a group; small incr. bronch. reac. in subgroup of asthmatics with >6% decr. FEV_1

APPENDIX IV. OVERVIEW OF OCCUPATIONAL ASTHMA.

Table 17-1

Occupational Asthma in United Kingdom 1989-91: Incidence Rates

Selected Occupational Group	Cases	Rate per Million per Year
Spray painters	108	729
Plastics workers	71	339
Chemical processors	75	337
Bakers	64	285
Laboratory workers	88	220
Metal treatment workers	51	211
Welders/electronics	106	158
Food processors	59	121
Hairdressers	24	81
Other painters	34	53
Farm workers	43	34

Table 17-2

Occupational Asthma in United Kingdom 1989-91: Main Causes

Cause	Number	Percentage
Isocyanates	326	22
Flour, grain, hay	108	7
Laboratory animals	87	6
Solder/colophony	85	6
Glues, resins	80	5
Wood	63	4
Other animals	61	4
Metals	58	4
Welding fume	35	2
Glutaraldehyde	30	2
Paints	29	2
Cutting oils	22	1
Inks and dyes	21	1

Table 17–3

Animal Causes of Occupational Asthma

Animal	Occupation
Rats, mice, guinea pigs, Rabbits	Laboratory workers, veterinarians
Horses	Veterinarians, stable hands
Prawns, crabs, sea squirt	Shell fish processors
Salmon, trout	Fish processing
Silkworm	Silk culture
Maggots	Fishermen
Storage mites	Farm, grain workers
Screw worm	Biological control work
River fly	Power station workers
Locusts	Laboratory workers
Chicken	Poultry workers
Pigeons, parakeets	Breeders

Table 17–4

Vegetable Causes of Occupational Asthma

Vegetable	Occupation
Flour	Bakers, millers
Grains	Farmers, distribution workers
Wood dusts	Joiners, sawyers, carpenters
Coffee bean	Processing and distribution workers
Castor bean	Processing and distribution workers
Soybean	Processing and distribution workers
Tea leaves	Processing and distribution workers
Tragacanth	Confectionery, pharmaceuticals
Gum acacia	Confectionery, pharmaceuticals
Latex	Production and use
Fungal spores and antigen	Farmers, biotechnology
Bacterial enzymes	Food technology, washing powder manufacture

Table 17–5

Chemical Causes of Asthma

Chemical	Occupation
Diisocyanates	Plastics, paints, adhesives
Acid anhydrides	Use of epoxy resins
Colophony	Soldering, electronics, metal machining
Amino ethyl ethanolamine	Aluminum jointing
Fluoride	Aluminum refining
Platinum salts	Refining, plating, jewelry
Cobalt and nickel	Hard metal manufacture and use, welding, plating
Chromium	Tanning
Vanadium	Oil-fired boiler cleaning
Antibiotics, Laxatives and other drugs	Manufacture
Powdered organic dyes	Textile dyeing
Paraphenylene diamine	Fur dyeing
Persulfate, henna	Hairdressing
Formaldehyde and glutaraldehyde	Nursing, laboratory work
Azodicarbonamide	Foam manufacture
Cyanoacrylate esters	Adhesive use
Cutting oils	Metal machining